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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,798	10/18/2000	Xavier Paliard	PP01521.101	3092

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EXAMINER
PURI, BEENA

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 12/28/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/673,798	Applicant(s) PALIARD, XAVIER	
	Examiner Beena Puri	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election group II (claim 1-4, 8, 10, 11, 16 -21, 23-24, 27-29) with traverse of Oct.1, 2001 in Paper No. 6 is acknowledged.

2. In response to the various species election, applicants elect HCV immuno-gens; and MIP-1alpha. Therefore, claim (s) 5-7, 9, 12-15, 22, 25-26 are withdrawn from further consideration by the examiner.

3. ***Response to Arguments***

Applicant's arguments filed on Oct.1, 2001 in Paper No. 6 is acknowledged as follows:

Group I: Claims 1-29, drawn to an immunogenic composition and a method of enhancing immune response wherein said method and composition comprise a chemokine (class 530, subclass 350, for example).

GroupII: Claims 1-29, drawn to an immunogenic composition and a method of enhancing immune response wherein said method and composition comprise a nucleic acid encoding a chemokine (class 435, subclass 325).

The inventions are distinct each from other as the proteins (chemokine) of invention I is different structurally and functionally from the nucleic acids of invention II. In addition, the proteins of invention I can be used materially different processes than

nucleic acids of invention II. For example, nucleic acids can be used as hybridization probes for screening cDNA and genomic libraries, and proteins can be used for antigen presenting cell priming. The differences between Invention I and II are further underscored by their divergent classification and independent search status.

Invention I is drawn to an immunogenic composition and a method of enhancing an immune response using chemokine proteins whereas invention II is drawn to an immunogenic composition and a method of enhancing an immune response using polynucleotide expressing chemokine.

The invention above have acquired a separate status in the art as a separate subject for inventive effect and require independent searches. The search for each of the above inventions is not co-extensive particularly with regard to the literature search. Further, a reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

4. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim(s) 1-4, 8, 10, 11, 16 -21, 23-24, 27-29, rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of enhancing an immune response for HCV DNA immunogen by co-administering a polynucleotide encoding macrophage inflammatory protein (MIP-1α) in baboon, does not reasonably provide enablement for other species of mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-4, 8, &10 are drawn to the immunogenic composition of DNA immunogen and polynucleotide encoding chemokine and further comprising a pharmaceutical acceptable carrier. Claims 11, 16-21, & 27-29 are drawn to a method of enhancing an immune response against DNA immunogen by administering polynucleotide encoding a chemokine in a mammal.

The nature of the invention is DNA vaccination against HCV and DNA are chosen from nonstructural genes of HCV. The specification teaches a route of delivery, dosage amount, frequency of administration, bleeding schedules with different plasmid DNA expressing HCV nonstructural polypeptides and polynucleotide expressing MIP-1α

a (Fig. 4) and also further teaches an enhanced immune response for said HCV non-structural DNA immunogens (Table 1 & 2) in the baboons. Thus the invention falls into the realm of non-viral approach of gene therapy.

At the time of filing, the relevant art considered gene therapy as a whole to be unpredictable as modes of delivery that would provide efficient delivery and expression of genes encoding the protein in the target cells had not been developed. This is not to say that the state of the art of gene therapy is in it's infancy and is highly unpredictable at the time of filing. **Mountain** (2000) recites " Naked DNA can be manufactured simply and cheaply in bacteria, an advantage that is magnified in strategies that require co-delivery of several genes. Its disadvantage include: 1) a gene delivery efficiency that is much lower than AD or AAV; 2) very brief expression in most tissues; and 3) unsuitability for targeting." The following references are cited herein to illustrate the state of art of immuno-therapy for HCV using DNA vaccine. There are two references most recently as year 1998 (same year as the applicants' priority date).

Trepo (1997) teaches that immune responses against Hepatitis C virus structural proteins following genetic immunization show humoral and cellular response in mice. They also recite a very weak response against DNA derived from HCV structural genes (See discussion, pg. 167). **Howard** (1998) recites nucleic acid vaccine against HCV in mice and DNA are prepared from the structural genes (See Abstract). Nakano (1997) teaches a humoral response for HCV E2 structural domain in mice. They recite that different route of injection can result in quantitatively and qualitatively different humoral immune response (See Abstract, pg. 7101). **Lagging** (1995) teaches humoral and

cellular immune response to DNA encoding the hepatitis C virus core protein in mice. References recited here demonstrate that DNA vaccine against HCV has been attempted against structural genes because structural genes are well known to be antigenic for humoral response and antibodies can prevent the infection. Also prior art shows that DNA vaccine is tested only in mice and shows different immune response in each case with different variables like vectors, routes, doses etc. There is no single reference for DNA vaccine derived from HCV nonstructural domain. In case of human papillomavirus vaccines, **Breitburd** (1999) recites that vaccination against nonstructural E1, E2, E6 or E7 viral proteins does not prevent infection (See abstract, pg. 431).

Thus, the relevant art considered for DNA vaccine as a whole to be unpredictable as modes of delivery that would provide efficient delivery and expression of genes encoding the nonstructural protein in the target cells had not been developed. An immune response to an immunogenic composition of DNA immunogen and polynucleotide encoding chemokine will vary from animal to animal in case of different species. Thus to overcome these teachings in the art, the specification would need to supply direct, correlative guidance as to administer HCV DNA immunogen and a polynucleotide encoding macrophage inflammatory protein (MIP-1α) in different species of mammals including human.

The breadth of the claims is very broad because claims 11, 16-21 & 27-29 are directed to a method of enhancing an HCV immune response in a mammal. The specification teaches that immune response against plasmid DNA expressing HCV nonstructural polypeptides is enhanced by co-administering polypeptide expressing

MIP-1α chemokine in the baboons. However, although animal models are valuable for the design of immune response, these models do not mimic relevant human conditions. The level of expression of said DNA plasmids will vary tremendously from animal to animal and animal to human. The amount of experimentation required to practice the claimed invention in other animals or human would necessiate undue experimentation on the part of one skilled in the art.

Thus the nature of the claimed invention, the level of predictability, the lack of working examples for using in more than one host, and the breadth of the claims, it is determined that one of skill in the art would need to practice a vast amount of experimentation in order to practice the invention commensurate in scope with the claims and this amount of experimentation is in fact undue.

5. Any inquiry concerning this communication from the examiner should be directed to Beena Puri, Ph. D. whose telephone number is (703) 306-0284. The examiner can normally be reached on Monday-Friday, 8:00 a.m. EST to 4:30 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051. The fax phone for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234. Question regarding review of formality issues may be directed to Kim Davis, the patent analyst assisting in this application. She may be reached at 703-305-3015.

Deborah Clark

DEBORAH J. R. CLARK
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Beena Puri, Ph.D.
Patent Examiner
Art Unit 1633
Oct. 25, 2001